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EXAMINER	
CELSA, BENNETT M	
ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

file copy

Office Action Summary	Application No. 09/181,108	Applicant(s) Miller et al.
	Examiner Bennett Celsa	Art Unit 1639

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 18, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-7, 10, and 42* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7, 10, and 42* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

Applicant's amendment and Declaration dated 7/18/03 in paper no.'s 28 and 29 are acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 1-7, 10 and 42 are pending and under consideration.

Election/Restriction

2. Applicant's election of Group I (original claims 1-10), with traverse in paper No. 10 and applicant's further election, without traverse, of the species of bis-N-[2-(2-aminomethyl)-1-methyl pyrrolidine]salicyladimanate Zinc II in Paper No. 13 which reads on claims 1-7 and 10 in response to the Supplemental Election of Species in paper no. 11 is again acknowledged.

Withdrawn Objection (s) and/or Rejection (s)

Applicant's arguments (e.g. metal complexes with only one non-biopolymer ligand) was found persuasive resulting in the withdrawal of the anticipation rejection of claims 1-7 under 35 U.S.C. 102(b) as being anticipated by Huc et al. PNAS USA Vol. 94 pages 2106-2110 (3/97) as well as the obviousness rejection of claims 1-7 and 10 under 35 U.S.C. 103(a) as obvious over Huc et al. alone or further in view of Benner, U.S. Pat. No. 5,958,702 (9/99: filed 2/95).

Outstanding Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 102 and 35 USC § 103

3. Claims 1-7, 10 and 42 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bruno et al. US Pat. No. 5,976,887 (11/99: filed 6/97) in view of the specification (e.g. page 10) cited in order to demonstrate the presence of functional properties inherent to the disclosed reference ligands. See MPEP 2131.01(d) which permits the citation of references or evidence in an anticipation rejection under 35 U.S.C. 102 in order to show that a characteristic not disclosed in the reference is inherent.

Bruno discloses the formation of combinatorial metal/ligand library complexes comprising aqueous equilibrium mixtures (e.g. see presence of deionized water in assay of example 1; or source of (transition) metal ions being wastewater, sewage etc: col. 1 and patent claims; i.e. which is "nondenaturing to a biological receptor") of 3 or more diaminoaromatic ligands (e.g. see 2/4 diaminotoluene; 3/4 diaminotoluene; 2/3 diaminotoluene: e.g. see patent claims 1,) and one or more metals (especially transition metals) (e.g. Au, Cu, Cr, Fe, Ru, Se and Va) to form combinatorial libraries of reversible metal/ligand complexes. The reference disclosure of tbe use of 17 metal ions (e.g. see Table 1) with two separate generics of substituted (with R)/unsubstituted diamino phenyl and substituted (withR)/unsubstituted naphythyl ligands would immediately envisage (e.g. anticipate) or in the alterative render obvious the making of a library of complex of 100 or greater [e.g. 17x 6(or more) phenyl ligands x 6(or more)naphthal ligands]. The formation of the metal reference complex ensure that the reference ligands possess "at least one functional

group capable of bonding to the metal atom" (e.g. an amino group). Additionally, all of the reference ligands inherently contain either unsubstituted or substituted (e.g. with amino or R) phenyl groups and thus comprise "a recognition group capable of binding a biological receptor" since recognition elements (e.g. DNA intercalators) include "substituted or unsubstituted phenyl groups" (e.g. see specification page 10, lines 4-5). Additionally, the reference ligands are "capable" of being modified to contain "recognition groups" within the scope of the presently claimed invention and thus would "comprise a recognition group *capable of* binding a biological receptor". It is noted that the reference complexes (e.g. see reference figures 1-13, especially figure 13) encompass the formation of complexes within the structural formula of present claims 1-7 and thus would be expected to inherently possess "a rate constant of greater than about 2 per second" since complexation does occur preferentially with the binding of 3 ligands/metal. However, in this regard it is noted that the Patent Office lacks the facilities for making comparisons between prior art and reference reaction kinetics; thus shifting the burden to applicant who is better able to make such comparisons.

Discussion

Applicant's arguments directed to the above anticipation rejection was considered but not deemed persuasive for the following reasons. It is first noted that the above rejection was modified in response to applicant's amendment.

Applicant argues that the effective 102(e) date of the Bruno reference is June 2, 1997 while the presently claimed invention was "reduced to practice in the U.S. prior to June 2, 1997 as evidenced by the accompanying Declaration of Benjamin L. Miller under 37 CFR 1.131.

The above argument and accompanying 1.131 Declaration were considered but not deemed persuasive for the following reasons.

First, the submitted 1.131 Declaration is improper since it must be made by all of the inventors and not just one inventor (e.g. Benjamin L. Miller). See e.g. MPEP 715.04.

Additionally, the 1.131 Declaration asserts reduction of practice citing the submission of the Klekota, Hammon and Miller JACS article. However, the article does not demonstrate reduction to practice of the disclosed/suggested species of the above-cited reference; nor does the one article library example (e.g. 36 bis salicyladiminato-zinc coordination complexes binding to double stranded oligo dT) demonstrate commensurate support for the presently claimed generic embodiment comprising diverse libraries of six or more different complexes comprising metal atoms/ions and at least two two non-biopolymer ligands which further comprise "a recognition element capable of binding a biological receptor". E.g. See MPEP 715.03

Accordingly, the above rejection is hereby maintained.

4. Claims 1-7, 10 and 42 are rejected under under 35 U.S.C. 103(a) as obvious over Jacobsen et al. WO 98/12156 (3/98) in view of Huc et al. PNAS USA Vol. 94 pages 2106-2110 (3/97) alone or if necessary further in view of Benner US Pat. No. 5,958,702 (9/99).

Jacobsen et al. disclose a combinatorial approach for generating novel coordination complex mixtures of "at least 6" (e.g. see page 6, lines 5-10) by coordinating to a transition metal (e.g. including zinc: see e.g.. Page 6, lines 17-26) and ligands (e.g. non-biopolymer: see e.g. pages 25-31) to form bidentate, tridentate, tetradentate or even higher order metal chelating ligands (e.g. see page 6, lines 7-10; and abstract). Additionally, a large number of the reference ligands (e.g. see pages 25-31) comprise substituted and unsubstituted aryl and heterocyclic moieties which would constitute "recognition elements" that are capable of being classed as "DNA intercalators" or "major or minor groove DNA binders" within the open ended specification definition of these terms (e.g. see specification pages 7-10 which encompass aryl and heterocycles as well as "hydroxy"; "alkoxy" or "amine" groups which are within the scope of the presently claimed invention) with these ligands being either phenyl or substituted derivative which further comprise an amine moiety. Alternatively , the selection of such an intercalating ligand would be obvious to one of ordinary skill in the art. See e.g. reference claims 29-30 and Fig. 1-11 disclose specific reference library combinations which are within the scope of the presently claimed invention.

Additionally, the Jacobsen reference also teaches that the reaction of the metal(s) with the library of PBM to form a combinatorial library of potential catalysts comprising metal complexes can occur in "solutions" (i.e. which are "nondenaturing to a biological receptor"), on a soluble support or utilizing insoluble polymeric supports (e.g. see page 39).

The Jacobsen reference making and screening of combinatorial solution phase library metal complexes differs from the presently claimed invention insofar that the presently claimed invention forms combinatorial libraries of complexes, such as those in Jacobson, in aqueous solution (e.g. non-denaturing to receptor) using "Receptor Assisted Combinatorial Chemistry" (aka RACC)..

The general application of "Receptor Assisted Combinatorial Chemistry" to generate libraries of "reversible" complexes for receptor screening in equilibrium under "physiological conditions" (e.g. aqueous) is taught by the Huc et al. reference (e.g.See Abstract and for aqueous environment: see Huc et al. at page 2107 right column: "reaction on which the library is based ... physiological conditions ... equilibrate in presence of receptor"; and on page 2108, left column in which the CA enzyme is present "in water at pH6"). For example, Huc et al. teach the making and screening (e.g. using "receptor-induced assembly" : see abstract and fig. 1) of a combinatorial library of "reversible" "labile" bonded complexes of "a plurality of at least six different complexes" (e.g. greater than or equal to 24 complexes: 4x6 plus enantiomers) under "physiological conditions" (e.g. in aqueous solution or suspension in equilibrium i.e. which additionally is "nondenaturing to a biological receptor") in the presence of "a biological receptor" (e.g. a transition metal Zn+2 & carbonic anhydrase: CAII) in which 4 or more amine ligands (e.g. a-d in Fig. 2) and 6 or more aldehyde/alcohol ligands are present in aqueous solution in the presence of CAII (e.g. Zn+2 and carbonic anhydrase). See Fig. 1-2; page 2107-2108. Such a technique results in the generation of large libraries which are most easily screened in solution. .

Additionally,, the Benner reference discloses the advantages of utilizing soluble "combinatorial library" techniques for generated diverse structures which could then be advantageously screened e.g. using a "receptor-assisted combinatorial chemistry" (e.g. see col. 2-5).. In this regard, the Benner reference discloses the versatility of this approach as utilized over a wide range of complexed atoms, groups of atoms or ions. In this regard, the Benner reference discloses the use of biopolymer or non-biopolymer ligands

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to apply RACC to the Jacobson transition metal and ligands (e.g. phenanthroline etc.) Libraries to generate complexes which contain "recognition elements" that are "capable of" binding a "target molecule" in solution (e.g. aqueous sol'n or suspension) in view of the advantages of utilizing combinatorial techniques (e..g increasing diversity) in solution (e.g. aqueous) as well as the advantages of utilizing improved screening techniques (e.g. receptor-assisted combinatorial chemistry) as disclosed in the Huc et al. reference taken alone or further in view of the Benner reference teaching.

Discussion

Applicant's arguments directed to the above anticipation rejection was considered but not deemed persuasive for the following reasons.

Applicant first that the Jacobson WO reference date for purposes of prior art is March 26, 1998 (under 35 USC 102a) and September 19, 1997 (under 35 USC 102e)

while the presently claimed invention was reduced to practice in the U.S. prior to June 2, 1997 as evidenced by the accompanying Declaration of Benjamin L. Miller under 37 CFR 1.131 thus removing the Jacobson reference as prior art. .

The above argument and accompanying 1.131 Declaration were considered but not deemed persuasive for the following reasons.

First, the submitted 1.131 Declaration is improper since it must be made by all of the inventors and not just one inventor (e.g. Benjamin L. Miller). See e.g. MPEP 715.04.

Additionally, the 1.131 Declaration asserts reduction of practice citing the submission of the Klekota, Hammon and Miller JACS article. However, the article does not demonstrate reduction to practice of the disclosed/suggested species of the above-cited reference; nor does the one article library example (e.g. 36 bis salicyladiminato-zinc coordination complexes binding to double stranded oligo dT) demonstrate commensurate support for the presently claimed generic embodiment comprising diverse libraries of six or more different complexes comprising metal atoms/ions and at least two two non-biopolymer ligands which further comprise "a recognition element capable of binding a biological receptor". E.g. See MPEP 715.03 Accordingly, the Jacobson WO document is still available as prior art.

Accordingly, the above rejection is hereby maintained

5. Claims 1-7, 10 and 42 are rejected under 35 U.S.C. 103(a) as obvious over Barton US Pat. No. 5,157,032 (10/92) in view of Huc et al. PNAS USA Vol. 94 pages 2106-2110 (3/97) alone or if necessary further in view of Benner US Pat. No. 5,958,702 (9/99) .

Barton discloses (chiral) reversible coordination complexes of transition metals which comprise "at least two non-biopolymer ligands" (e.g. three ligands which comprise unsubstituted/substituted 1,10 phenanthrolines, racemers and isomers) which contain a "recognition element" which "targets" DNA (e.g. see abstract, examples and patent claims, especially patent claim 1).These complexes (and their isomers: e.g. see col. 11) bind (in assays) DNA (e.g. "contain a recognition element capable of binding a receptor") without denaturing the DNA. For example, Barton discloses a cobalt complex with ligands which comprise 1,10 phenanthroline and a list of 12 "substituted" phenanthrolines" (e.g. hydroxy, phenyl, substituted phenyl intercalotors etc.) which include their racemers (e.g. see col. 7, lines 1- 40) which would encompass at least 169 distinct complexes (e.g. 13x13 representing 13 unsubstituted and substituted and their D/L enantiomers). These complexes are then screened for their binding to a "receptor" (e.g. DNA) by intercalation: see. bottom of col. 7 to top of col. 8).

The Barton reference composition differs from the presently claimed invention insofar that the presently claimed invention forms combinatorial libraries of complexes, such as those in Barton, in aqueuos solution (nondenaturing to the receptor) using "Receptor Assisted Combinatorial Chemistry" (aka RACC)..

The general application of "Receptor Assisted Combinatorial Chemistry" to generate libraries of "reversible" complexes for receptor screening in equilibrium under "physiological conditions" (e.g. aqueous) is taught by the Huc et al. reference (e.g.See Abstract and for aqueous environment: see Huc et al. at page 2107 right column: "reaction on which the library is based ... physiological conditions ... equilibrate in presence of receptor"; and on page 2108, left column in which the CA enzyme is present "in water at pH6"). For example, Huc et al. teach the making and screening (e.g. using "receptor-induced assembly" : see abstract and fig. 1) of a combinatorial library of "reversible" "labile" bonded complexes of "a plurality of at least six different complexes" (e.g. greater than or equal to 24 complexes: 4x6 plus enantiomers) under "physiological conditions" (e.g. in aqueous solution or suspension in equilibrium i.e. which is "nondenaturing to a biological receptor") in the presence of "a biological receptor" (e.g. a transition metal Zn+2 & carbonic anhydrase: CAII) in which 4 or more amine ligands (e.g. a-d in Fig. 2) and 6 or more aldehyde/alcohol ligands are present in aqueous solution in the presence of CAII (e.g. Zn+2 and carbonic anhydrase). See Fig. 1-2; page 2107-2108. Such a technique results in the generation of large libraries which are most easily screened in solution. ..

Additionally, the Benner reference discloses the advantages of utilizing soluble "combinatorial library" techniques for generated diverse structures which could then be advantageously screened e.g. using a "receptor-assisted combinatorial chemistry" (e.g. see col. 2-5).. In this regard, the Benner reference discloses the versatility of this approach as utilized over a

wide range of complexed atoms, groups of atoms or ions. In this regard, the Benner reference discloses the use of biopolymer or non-biopolymer ligands

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to apply RACC to the Barton generic of transition metal and ligands (e.g. phenanthroline etc.) to generate complexes which contain "recognition elements" that are "capable of" binding a "target molecule" (e.g. DNA) in solution (e.g. aqueous sol'n or suspension) in view of the advantages of utilizing combinatorial techniques (e..g increasing diversity) in solution (e.g. aqueous) as well as the advantages of utilizing improved screening techniques (e.g. receptor-assisted combinatorial chemistry) as disclosed in the Huc et al. reference taken alone or further in view of the Benner reference teaching.

Additionally, scaling the library up by increasing the number of library members (e.g. increase the number of Barton substituted phenanthroline ligand) to attain increased diversity is suggested by both the Huc et al. And Benner references, taken separately or in combination, and would in any event represent mere optimization to one of ordinary skill in the art.

Discussion

Applicant's arguments directed to the above obviousness rejection were considered but deemed nonpersuasive.

Applicant argues that the Barton reference coordination complexes are prepared individually and under non-aqueous (and often denaturing) conditions referring to preparation examples I-III.

This argument is not persuasive for the following reasons.

In response to applicant's arguments against the Barton reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). As pointed out in the rejection above: " The Barton reference composition differs from the presently claimed invention insofar that the presently claimed invention forms combinatorial libraries of complexes, such as those in Barton, in aqueuos solution (e.g. non-denaturing to the receptor) using "Receptor Assisted Combinatorial Chemistry" (aka RACC)".

Additionally, the Examiner is confused as to what (receptor e.g. DNA) denaturing conditions applicant is asserting is "often" taught by the Barton reference since the Barton reference clearly conducts assays with DNA and the complexes under non-denaturing conditions.

Applicant further argues that contrary to the PTO's suggestion "... the complexes formed by Barton are not characterized by the presence of a labile bond between the ligand and the transition metal ion" and "[T]he resulting coordination complexes are stable di- or tri-cations-they are described as chloride salts in the Examples-and therefore would not be expected to exist at equilibrium with the component transition metal ions and ligands when introduced into an aqueous environment".

Applicant's argument is not persuasive for several reasons.

The Barton reference clearly discloses at least six different complexes that comprise coordinately bound metals (ions/atom) and "non-biopolymer ligands" within the scope of the presently claimed invention (E.g. see Barton abstract; figures and patent claim 1) and are thus capable of ligand exchange when placed in aqueous solution as motivated by the teaching of the Huc et al. and/or Benner references. Accordingly, applicant's arguments fails to address the full scope (which is not limited to specific salt examples) of the Barton reference teaching (e.g. see patent claim 1) of reference complexes; nor is applicant's arguments commensurate in scope with the presently claimed invention. Additionally, applicant has failed to point out what critical core structure (not present in the present claims) is lacking in the disclosed and claimed Barton coordination complexes which necessarily renders the prior art coordinate bounds "non-labile" or "irreversibly bonded" and thus outside the scope of the presently claimed invention. To the extent that the Barton compounds assertedly lack such properties (which is disputed by the Examiner); applicant's claims fail to provide the necessary core structure (e.g. ligands; metals; charge etc.) which necessarily results in such properties. In this regard it is also noted that the PTO lacks the necessary facilities to compare prior art compounds with those compounds within the claim scope; and mere attorney argument cannot substitute for factual evidence. .

Applicant further argues in summary that the Barton reference teaches away from making a combinorial library using receptor assisted combinatorial chemistry since the Barton double stranded DNA (dsDNA) could not tolerate the non-aqueous and/or denaturing conditions used during individual complex syntheses.

Applicant's argument is not persuasive for several reasons.

Initially, it is noted that applicant's denaturing argument is only applicable against new claim 42; but is not relevant agains the remaining claims which lack such a limitation.

More importantly applicant's argument fails to address the rationale of motivation to combine the references in the above rejection ; e.g. the use of the receptor assisted combinatorial chemistry for its intended purpose e.g. the screening of a prospective library of complexes with a receptor (E.g. DNA) for purposes of determining the complex with the *highest DNA binding affinity*.

Additionally, contrary to applicant's denaturation argument.Barton clearly utilizes its complexes and resulting libraries in assays under non-denaturing DNA conditions. In this regard, Barton clearly teaches that its complexes and resulting **libraries** (e.g 2 or more members include racemers) bind DNA (e.g. in an assay) under NON-denaturing DNA conditions (e.g. "used to selectively label a conformation": e.g. see col. 5) since *conformational integrity* (NO DENATURATION CAN OCCUR) and DNA binding are a prerequisite to use of the Barton complexes and libraries resulting therefrom. Accordingly, denaturation conditions are necessarily not present when the Barton complexes are being bound to the DNA.

Applicant argues that the Barton reference fails to teach aqueous complex formation using receptor assisted combinatorial chemistry.

In response to applicant's arguments against the Barton reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant further argues that there is not a reasonable expectation of success for conducting receptor assisted combinatorial chemisry to prepare Barton's complexes since there is no evidence that such complexes contain labile bonds and the secondrary reference fail to teach reaction conditions for conducting receptor assisted combinatorial chemistry of the Barton compounds.

This argument is nonpersuasive for several reasons.

Applicant's argument regarding labile bonds was addressed in detail above and is herein incorporated by reference in its entirety. Suffice it to say that Barton's complexes are clearly within the structural scope of the presently claimed invention and applicant has failed to provide any scientific rationale (e.g. critical core structure; metal charge etc.) as to why such coordinate complexes would necessarily possess *irreversible nonlabile* coordinate bounds.

Applicant's second point that the none of the reference teach receptor assisted combinatorial chemistry of the Barton's compounds is evidenced by raising of an obviousness rejection (and not anticipation) in the present context.

Regarding, nonenablement Applicant has failed to provide a scientific rationale as to why one of ordinary skill in the art would have difficulty combinatorially synthesizing and screening compounds where the recited references provide the compounds as well as synthetic and screening protocols. It is noted that obviousness does not require absolute certainty; but only a

reasonable expectation which is clearly present in the combined teaching of the above-cited references.

Accordingly, the above-cited obviousness rejection is hereby maintained.

New Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 112

6. Claim 42 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (e.g. NEW MATTER REJECTION) .

In new claims 42 the phrase "the **aqueous solution or suspension**, in which the combinatorial library exists, **is non-denaturing to a biological receptor**" (emphasis provided)is not supported in the specification and applicant has failed to indicate where said support exists. It is noted that the specification on page 16 (bottom) references to light/temperature (external to solution) biological receptor sensitiby fails to provide specific or commensurate support for "non-denaturing" solution/suspension non-denaturing conditions as presently claimed.

7. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term " the aqueous solution or suspension, in which the combinatorial library exists, is non-denaturing to a biological receptor"" in claim 42 lacks metes and bounds and is therefore indefinite as to what other aqueous solution/suspension parameters/conditions, besides temperature/light are encompassed by the presently claimed invention for the broad scope (DNA/PROTEIN/CARBOHYDRATE etc) of biological receptors.

Conclusion

8. **Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).**

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang (art unit 1639), can be reached at (703)306-3217.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1639)
September 26, 2003

BENNETT CELSA
PRIMARY EXAMINER